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## Are photosensitizing medications associated with increased risk of important erythematous reactions during ultraviolet B phototherapy?

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**Are photosensitising medications associated with increased risk of important erythematous reactions during UVB phototherapy?**

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Accepted Article

Dear Editor, Erythematous episodes during phototherapy can be painful, limit efficacy due to premature discontinuation of treatment and may contribute to chronic cutaneous damage. Many patients receiving phototherapy take photosensitive medications. Stern *et al.*, investigated 1,125 patients receiving maintenance psoralen-ultraviolet A photochemotherapy (PUVA) for psoriasis and did not detect a significant difference in risk of erythematous episodes between those receiving photosensitising medication compared with those who were not<sup>1</sup>. However, amongst older ( $\geq 45$  years-old) users of photoactive drugs, 10% discontinued PUVA for at least a month because of “burns” compared with only 5% on “non-users”.

In Tayside, a study of 401 patients receiving narrowband ultraviolet B phototherapy (NB-UVB) revealed that some photosensitising medications, particularly calcium channel antagonists, phenothiazines and non-steroidal anti-inflammatories (NSAIDs), were associated with a lower baseline minimal erythema dose (MED)<sup>2</sup>.

In this current retrospective cohort study, we investigated whether patients taking photosensitising drugs were more at risk of developing significant erythematous episodes during NB-UVB phototherapy than those who were not.

All patients receiving NB-UVB phototherapy to at least photo-exposed sites between January 2012 and December 2015 in the Dundee phototherapy unit were studied. Caldicott Guardian Approval was obtained. Exclusion criteria included patients receiving phototherapy for photodermatoses or vitiligo and those who received  $<10$  or  $>200$  sessions. Patients with erythema not formally graded (mainly those receiving home NB-UVB) and those with an ambiguous medication history were excluded. Erythematous episodes were included if they were at least grade 2 (well-demarcated and uncomfortable). Grade 3 erythema was defined like grade 2 but definitely painful and grade 4 as severe with blisters. Erythema considered to be from outdoor exposure was discounted. This information was obtained from Photosys, the database of the National Managed Clinical Network for Phototherapy in Scotland and the patients’ phototherapy notes.

Potentially UVB photosensitising medication groups evaluated were NSAIDs, thiazide and loop diuretics, retinoids, sulfonyleureas, phenothiazines, H<sub>2</sub> antagonists, calcium channel antagonists, tricyclic antidepressants, tetracyclines and quinine.

There were 1067 NBUVB phototherapy courses, in 880 patients, fitting the above criteria. Most (702) were single patient courses, but 365 were repeated courses in individual patients (maximum 4 courses). Mean age was 46 (range 6-90) years and 50.2% of courses were for females. Skin phototype II predominated (53.4% of courses), with skin phototype VI being the least frequent (0.1% of courses). Psoriasis was the most common indication for phototherapy (54.6% of courses).

The median number of treatments per course was 28 (range 10 to 98). The median MED was 0.139J/cm<sup>2</sup> (range 0.025-3.53J/cm<sup>2</sup>) with no detectable difference between MED for the photosensitising drug group and the control group.

Of the 56 grade 3 and 4 reactions, 53.6% were localised. The face was the most common site, accounting for 30% of localised cases.

There were 276 courses during which patients taking potentially photosensitising medication (25.9%) and 42% of this group experienced an erythematous episode of grade 2, compared with 36% of controls, that is 6% more (95% confidence interval 0% to 13%; p=0.06) (Figure 1).

Patients receiving photosensitising medication were also more likely to have an erythematous episode of grade 3 (7.2%) than controls (3.2%), that is 4% more (95% confidence interval for difference 1% to 7%; p=0.0053) had severe erythematous episodes in the photosensitising drug group (Figure 1).

There was a total of only 4 grade 4 episodes in all courses, demonstrating that grade 4 erythema is a rare event whether on or off photosensitising drugs.

Patients receiving UVB courses and concomitant quinine ingestion were most likely to develop an erythematous episode of grade 2 or above (83.3% of those on quinine [n=6]), followed by those taking tetracyclines (68.8% of those on tetracyclines [n=16]) and tricyclic antidepressants (62.1% of those on these drugs [n=37]).

There was no detectable difference between number of erythematous episodes recorded and the number of classes of photosensitising medication a patient was taking.

This study suggests that, despite using starting doses based on an individual's NB-UVB MED, patients taking photosensitising medication were still more likely to develop important (grade 2 or more) erythematous episodes during NB-UVB phototherapy. It is therefore essential that a detailed drug history is taken prior to commencement of phototherapy, in addition to establishing a baseline MED and that any medication changes during treatment are highlighted. Although these medications were associated with more important erythemas, the proportion who developed severe erythema was low. It is important that patients are not deprived of the opportunity of phototherapy because of their medication, although potentially photosensitising medication should be stopped whilst a patient is undergoing phototherapy when possible. Patients should be counselled about this increased risk of erythema with photosensitising drugs during phototherapy and should be encouraged to report medication changes. While the dosing incremental change remains the same as those not on photosensitive medication, it could be adjusted for those on photosensitizing medication experiencing erythematous reactions.

## References:

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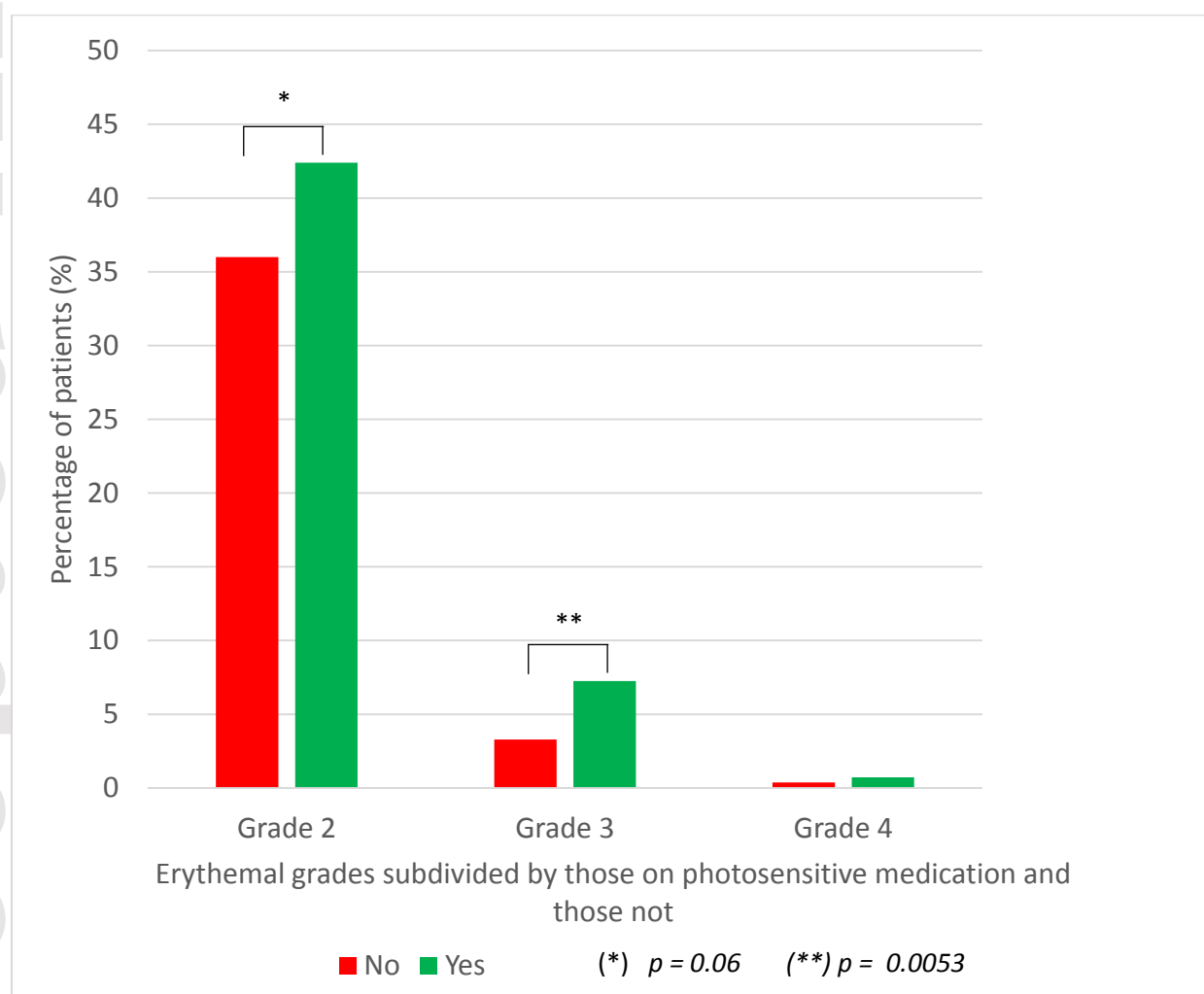


Figure 1: Percentage of courses associated with erythema episodes in those receiving photosensitising medication and in the control patient group